CRD summary
This review concluded that there is insufficient evidence to recommend the routine use of ondansetron for vomiting during acute gastroenteritis in children, despite some clinical benefits. There were considerable limitations to this review but, overall, the authors’ conclusion appears reasonable and the recommendations for future research seem justified.

Authors’ objectives
To determine the effects of ondansetron for the treatment of vomiting during acute gastroenteritis in children.

Searching
MEDLINE (1966 to August 2006), EMBASE (1980 to August 2006), CINAHL (1982 to August 2006), the Cochrane Database of Systematic Reviews (Issue 3, 2006) and the Cochrane Controlled Trials Register (Issue 3, 2006) were searched; the search terms were reported. No language restrictions were imposed. Only full publications were eligible for inclusion. Abstracts, letters to editors and conference proceedings were excluded. The reference lists in identified studies and review articles were screened.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion. Only studies with more than 80% follow-up were included.

Specific interventions included in the review
Studies evaluating ondansetron compared with placebo or no intervention were eligible for inclusion. The dosage and route of administration of ondansetron varied between studies: 0.3 mg/kg, single dose administered intravenously; 2 to 8 mg depending on body weight, taken orally as a single dose; 1.6 to 4 mg/kg depending on age, six doses taken orally; 0.15 mg/kg (maximum 8 mg), single dose administered intravenously.

Participants included in the review
Studies of children with gastroenteritis were eligible for inclusion. All of the included participants were experiencing acute gastroenteritis, but the definition varied between studies. In the majority of studies the age of the participants ranged from 6 months to 8 or 12 years; in one the participants were aged from 1 month to 22 years.

Outcomes assessed in the review
Studies measuring cessation of vomiting, need for intravenous rehydration, hospitalisation, return visit to emergency department (ED), intake of oral rehydration solutions (ORS), length of stay in the ED and adverse events were eligible for inclusion.

How were decisions on the relevance of primary studies made?
Three reviewers independently selected studies and resolved any disagreements through consensus.

Assessment of study quality
Reviewers independently assessed study quality on the basis of allocation concealment, blinding of the investigators, participants, outcome assessors and data analysts, intention-to-treat analysis and comprehensive follow-up. The methods defined in the Cochrane Handbook for Systematic Reviews of Interventions 4.2.5 (updated May 2005) were used.
Data extraction

Three reviewers independently extracted the data onto a standardised form and resolved any disagreements through consensus. In studies with multiple experimental arms, only data on ondansetron were included.

Methods of synthesis

How were the studies combined?

A meta-analysis was used to estimate the pooled risk ratio (RR) and risk benefit with 95% confidence intervals (CIs). A fixed-effect model was used when there was no evidence of statistical heterogeneity; results obtained using a random-effects model were also reported where heterogeneity was observed. The number-needed-to-treat (NNT) was calculated.

Publication bias was not formally assessed because of the small number of studies, as the authors stated that any formal method would lack power.

How were differences between studies investigated?

Heterogeneity was assessed using the chi-squared and I-squared statistical tests.

Results of the review

Four RCTs (n=490) were included in the review.

Generation of allocation sequence and allocation concealment was adequate in 3 studies and unclear in the fourth; double-blinding was utilised in all studies. Less than 20% of the participants were lost to follow-up in the included studies.

Cessation of vomiting.

There was a greater likelihood of cessation of vomiting during the first hours in the ondansetron group compared with the placebo group (RR 1.33, 95% CI: 1.33, 1.50, p<0.00001; 3 studies, n=466); the NNT was 5 (95% CI: 4, 8). There was no evidence of statistical heterogeneity in this group. However, there were no statistically significant differences between the ondansetron and control groups for cessation of vomiting within 24 hours (RR 1.22, 95% CI: 0.89, 1.67; 2 studies, n=144), but these studies demonstrated significant statistical heterogeneity (I-squared 55.5%).

Intravenous rehydration.

The ondansetron group showed a reduction in the risk of intravenous rehydration in comparison with those in the placebo group (RR 0.42, 95% CI: 0.27, 0.67, p=0.0003; 2 studies, n=359); the NNT was 7 (95% CI: 5, 14). There was no evidence of statistical heterogeneity in this group.

Hospitalisation.

There was no statistically significant risk of hospitalisation in the ondansetron group compared with the placebo group (RR 0.6, 95% CI: 0.2, 1.4; 3 studies, n=466).

Return visit to the ED.

There were no statistically significant differences between groups in terms of return visits to the ED (RR 1.3, 95% CI: 0.8, 2.2).

ORS intake.

There was an increased intake of ORS in ondansetron compared with the placebo group (mean difference 43 mL, 95% CI: 15.5, 70.5; 1 study, n=214), although the same study showed no significant difference in duration in the ED.

Diarrhoea.
One study showed a significant difference between the ondansetron and placebo groups in the number of episodes of diarrhoeal stools while in the ED, whereas a second study showed no difference (data not reported). Two studies showed significantly more episodes of diarrhoea at the 24-hour follow-up in the ondansetron group compared with the placebo group (data not reported). One trial showed the same effect between the ondansetron and placebo groups at the 48-hour follow-up (data not reported).

Adverse events.

Ondansetron was well tolerated (3 studies, n=345) and adverse events were similar in both groups (data not reported).

Authors’ conclusions
There is insufficient evidence to recommend the routine use of ondansetron for vomiting during acute gastroenteritis in children, despite some clinical benefits.

CRD commentary
The review addressed a clear question in terms of the participants, interventions, outcomes and study design. Several databases were searched, the search terms and dates were reported, and no language restrictions were applied, thus limiting the possibility of publication bias. However, the authors did not formally assess publication bias because of the small number of included studies. Methods were used to minimise reviewer error and bias in the study selection and data extraction processes. Validity was assessed using published criteria.

There was evidence of clinical heterogeneity between the studies. For example, one review included participants from 1 month to 22 years of age, making it difficult to assess the effectiveness of the intervention only in children. The dosage and route of administration, as well as outcome definitions, also varied considerably between the studies. Where there was clinical and statistical heterogeneity, combining the studies in a meta-analysis might not have been appropriate. There were considerable limitations to this review but, overall, the authors’ cautious conclusion appears reasonable and the recommendations for future research seem justified.

Implications of the review for practice and research
Practice: The authors stated that there is insufficient evidence to recommend the routine use of ondansetron for the treatment of vomiting in children with acute gastroenteritis if a child is at low risk for dehydration.

Research: The authors stated that further well-conducted clinical trials using validated outcomes are needed to assess the effectiveness and cost-effectiveness of using ondansetron to treat children with acute diarrhoea, and to determine subgroups deriving greatest clinical benefit from the treatment.

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